I hereby certify that this correspondence is being electronically filed in the United States Patent and Trademark Office on March 27, 2009.

Frank C. Eisenschenk, Ph.D., Patent Attorney

REQUEST FOR CERTIFICATE OF CORRECTION UNDER 37 CFR 1.322 AND UNDER 37 CFR 1.323
Docket No. ST.101XT
Patent No. 7,452,987

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Klaus Giese, Jorg Kaufmann, Anke Klippel-Giese
Issued	:	November 18, 2008
Patent No.	:	7,452,987
Conf. No.	:	6369
For	:	Interfering RNA Molecules

Mail Stop Certificate of Corrections Branch
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REQUEST FOR CERTIFICATE OF CORRECTION
UNDER 37 CFR 1.322 (OFFICE MISTAKE)
UNDER 37 CFR 1.323 (APPLICANT MISTAKE)

Sir:

A Certificate of Correction for the above-identified patent has been prepared and is attached hereto.

In the left-hand column below is the column and line number where errors occurred in the patent. In the right-hand column is the page and line number in the application where the correct information appears.

Patent Reads:	**Application Should Read:**
Column 4, line 44:	Page 6, lines 25-26:
"bases In"	--bases. In--
Column 5, line 49:	Page 8, line 18:
"using a he ribonucleic"	--using a ribonucleic--

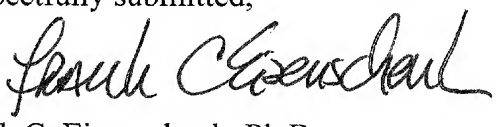
Column 6, line 20:	Page 9, lines 12-13:
"of the a ribonucleic"	--of a ribonucleic--
Patent Reads:	**Application Reads:**
Column 6, line 28:	Page 9, line 17:
"MRNA."	--mRNA.--
Patent Reads:	**Application Should Read:**
Column 8, line 24:	Amendment in Response to Notice Under 37 CFR §§1.821-825 dated February 4, 2004:
"101-1118,"	--101-118,--
Column 10, line 66:	Page 15, line 32:
"may added"	--may be added--
Column 16, line 59:	Page 25, line 1:
"group of nucleotide"	--group of nucleotides--
Patent Reads:	**Application Reads:**
Column 23, line 36:	Page 34, line 27:
"1 8A"	--18A--
Patent Reads:	**Application Should Read:**
Column 29, line 52:	Page 43, line 21:
"72,"	--72 h,--

A true and correct copy of pages 9 and 34 of the specification as filed which support Applicants' assertion of the errors on the part of the Patent Office accompanies this Certificate of Correction.

The fee of $100.00 was paid at the time this Request was filed. The Commissioner is also authorized to charge any additional fees as required under 37 CFR 1.20(a) to Deposit Account No. 19-0065.

Approval of the Certificate of Correction is respectfully requested.

Respectfully submitted,



Frank C. Eisenschenk, Ph.D.
Patent Attorney
Registration No. 45,332
Phone No.: 352-375-8100
Fax No.: 352-372-5800
Address: P.O. Box 142950
Gainesville, FL 32614-2950

FCE/jnw

Attachments: Copy of pages 9 and 34 of the specification

In accordance with a ninth aspect of the present invention there has been provided a composition containing a ribonucleic acid according to any of the aspects of the present invention.

In accordance with a tenth aspect of the present invention there has been provided a pharmaceutical composition containing a ribonucleic acid according to any of the aspects of the present invention, and a pharmaceutically acceptable carrier.

In accordance with an eleventh aspect of the present invention there has been provided a method for inhibiting the expression of a target gene in a cell or derivative thereof comprising introducing a ribonucleic acid according to any of the aspects of the present invention into a cell in an amount sufficient to inhibit expression of the target gene, wherein the target gene is the target gene of the a ribonucleic acid according to any of the aspects of the present invention.

Brief Description of the Drawings

Fig. 1 shows a schematic illustration defining the terminology as used herein. The upper of the two strands is the first strand and the antisense strand of the targeted nucleic acid such as mRNA. The second strand is the one which essentially corresponds in its sequence to the targeted nucleic acid and thus forms the sense strand. Both, the first strand and second strand form a double-stranded structure, typically through Watson Crick base pairing.

Fig. 2 illustrates some embodiments of the ribonucleic acid molecules of the present invention with patterns of modified and unmodified groups of nucleotides which are also referred to herein as a pattern of modification. The modified groups of nucleotides are also referred to herein as a group of modified nucleotides. The unmodified nucleotides or unmodified groups of nucleotides referred to as flanking group(s) of nucleotides herein, as used herein may also have one or several of the modification(s) as disclosed herein which, however, is/are different from the modification of the nucleotides forming the group(s) of modified nucleotides. In Fig. 2A the modified and unmodified groups of nucleotides, *i.e.* the groups of modified nucleotides and the flanking groups of nucleotides on both the first stretch and the second stretch are located on corresponding parts of the stretches and are thus aligned to each other (groups of modified nucleotides on the first strand aligned with groups of modified nucleotides on the second strand and flanking groups of nucleotides on the first

modification to stabilize or with other beneficial properties (delivery) will be tolerated without activity loss when located at the 3' OH; especially when the 3'OH is located on an overhanging nucleotide.

For the experiment shown in Fig. 3C similar conditions as outlined above were used. The first strand and the second strand of the RNAi were either modified by a NH_2 group at the 3'-position of the ribose moiety or by an inverted abasic at said positions. The first construct is designated as siRNA-NH_2 (3A3B) the second as siRNA-iB (4A4B). The sequence of both molecules is depicted in Fig. 3B. The term 3A3B indicates that the interfering ribonucleic acid consists of strand 3A as the antisense strand and strand 3B as the sense strand. For reason of comparison an antisense oligonucleotide designated GB53 (Sternberger et al., supra) was generated which was directed against the PTEN mRNA as well. The particularities of this latter experiment were as follows.

As may be taken from Fig. 3C end protected RNAi molecules depicted in Fig. 3B are functional in yielding a PTEN protein knockdown.

From this example it can be taken that both end protection groups render RNAi molecules active in knocking down PTEN protein. This inhibition is as efficient as inhibition with antisense constructs but at lower concentrations used which is a clear advantage over the already very powerful antisense technology.

Example 2: Overhang requirements for RNAi duplex activity in vivo

The experimental procedures were the same as depicted in connection with Example 1 except that the PTEN mRNA targeting interfering RNAi molecules were differently designed. The results are shown in Fig. 4A as dose response curves with Fig. 4B showing the particular sequence and modifications of the interfering RNAi molecules used to generate the data depicted in Fig. 4A. The nomenclature is such that, *e.g.*, RNAi 18 is composed of strand 18A as antisense strand and strand 18B as sense strand.

Blunt ended molecules were compared to molecules with 3'-overhangs (RNAi 18) and 5'-overhangs (RNAi 30 and RNAi 31) in their activity to knockdown PTEN mRNA in HeLa cells. The activity of blunt ended molecules (RNAi 28) and molecules with 5'-overhangs was comparable to the activity of molecules with 3'-overhangs. This shows that 3'-overhangs are not required for RNAi activity.

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 7,452,987

APPLICATION NO.: 10/633,630

DATED : November 18, 2008

INVENTOR : Klaus Giese, Jorg Kaufmann, Anke Klippel-Giese

It is certified that errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 4,
Line 44, "bases In" should read --bases. In--.

Column 5,
Line 49, "using a he ribonucleic" should read --using a ribonucleic--.

Column 6,
Line 20, "of the a ribonucleic" should read --of a ribonucleic--.
Line 28, "MRNA." should read --mRNA.--.

Column 8,
Line 24, "101-1118," should read --101-118,--.

Column 10,
Line 66, "may added" should read --may be added--.

Column 16,
Line 59, "group of nucleotide" should read --group of nucleotides--.

Column 23,
Line 36, "1 8A" should read --18A--.

Column 29,
Line 52, "72," should read --72 h,--.

MAILING ADDRESS OF SENDER:
Saliwanchik, Lloyd & Saliwanchik
P.O. Box 142950
Gainesville, FL 32614-2950